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# FOREWORD

The Venereal Disease Program of the Division of Special Health Services desires to assist in the solution of any problem in the management of venereal disease. Resources of the Program include: research activities through its research laboratories, publication services through its editorial staff, educational materials, exhibits, visual aids, reference services, statistical services, and laboratory and interviewing training facilities for clinicians, technicians, nurses, and interviewers.

The "VD Fact Sheet" is published yearly and the "Directory of Venereal Disease Clinics," every two years. Among the publications of the Program which have been especially popular with physicians are: "Serologic Tests for Syphilis, 1955 Manual," PHS Publication 411; "The Diagnosis of Syphilis by the General Practitioner," PHS Publication 426; "Management of Chancroid, Granuloma Inguinale, and Lymphogranuloma Venereum in General Practice," PHS Publication 255; "Autopsy Studies in Syphilis," PHS Publication 433; and "Nursing in Venereal Disease Control," PHS Publication 198. Many articles by members of the Program staff appear in "Public Health Reports." Abstracts of articles on venereal disease from approximately 300 English-language medical journals are published under the title, "Current Literature on Venereal Disease." These are indexed annually.

Information about any service of the Program is available upon request to the Chief, Venereal Disease Program, Division of Special Health Services, U. S. Public Health Service, Washington 25, D. C.

Note: While procaine penicillin G in oil with 2 percent aluminum monostearate (PAM) and benzathine penicillin G are recommended here, as other types of delayed action preparations are developed and evaluated they may prove equally useful or even superior.

Schedules for treatment of primary and secondary syphilis are based upon experience of the Venereal Disease Program. The schedules for other stages of syphilis and other venereal diseases are based upon experience of various workers, and have been used satisfactorily by the treatment centers of the Public Health Service. They include the latest information available on June 1, 1955.

Trade names are used for identification only and do not represent an endorsement by the Public Health Service.

## EPIDEMIOLOGIC TECHNIQUES

In the management of all forms of venereal disease, it is recommended that certain public health techniques be followed carefully in addition to treatment of patients. For each patient having a venereal disease treated, the case report forms required by the State or local health department should be submitted. In view of the extremely important role of contact investigation in control of venereal disease it is recommended that every effort be made to secure adequate contact information from each patient treated. Consultation on interviewing techniques and assistance in procuring trained contact interviewers can be secured through your local health department or through your State department of health.

## MANAGEMENT OF GONORRHEA

Gonorrhea

Laboratory Diagnosis:
- In the female - by culture
- In the male
  - Acute gonorrhea - by culture or by smear
  - Chronic gonorrhea - by culture

Treatment:
- Uncomplicated gonorrhea - procaine penicillin G in oil with 2 percent aluminum monostearate (PAM) or benzathine penicillin G, 600,000 units in one intramuscular injection
- Gonorrhea with complications (eye involvement, prostatitis, arthritis, etc.) - aqueous penicillin G, 600,000 to 1,200,000 units per day at 2- to 4-hour intervals or equivalent amounts of repository penicillin until signs and symptoms have subsided

Re-treatment:
- If discharge in uncomplicated gonorrhea persists for 3 days or more after initial treatment and smear or culture still is positive, re-treat with single injection of 1,200,000 units or two injections of 600,000 units on alternate days

Serologic Test for Syphilis (STS):
- Before treatment and monthly for 4 months following treatment

The diagnosis of gonorrhea is confirmed by culturing the organism from fresh secretions. For routine purposes, simple identification of typical gram-negative intracellular diplococci in a stained spread of purulent discharge material generally is sufficient for the diagnosis of acute gonorrhea in the male. Only the culture is considered of value in chronic gonorrhea or in gonorrhea in the female. "Procedures for Isolation and Identification of the Gonococcus" * provides detailed information on laboratory diagnostic procedure.

If relapse occurs it usually will be seen in the first week after treatment. It occasionally is found that what appears to be penicillin resistance is a reinfection contracted from a regular sex partner who has not been given treatment or who is undiscovered for lack of proper epidemiologic studies. In patient management and in diagnosis it is important to remember that penicillin resistant strains of gonococci have not yet been seen in vivo.

Examination for evidence of residual gonococcic infection may be done about 7 days after completion of therapy. The test of cure, if done at all, should consist of cultures. For the male, a test of cure is considered unnecessary in the absence of signs or symptoms.

In posttreatment follow-up of acute gonorrhea in the male, instrumentation as an aid in determining the presence of gonorrhea is not necessary and is not advised. If there is prolonged persistence of a discharge after treatment of the patient and all his contacts, reevaluation and genitourinary consultation are indicated.

Occurrence of chills and fever (Herxheimer reaction) in patients receiving treatment for gonorrhea is strongly suggestive of a concurrent infection with syphilis. In such patients, treatment should be prolonged to provide a complete course for syphilis as outlined under treatment of primary syphilis. The definitive diagnosis of syphilis is not warranted on the evidence of a presumed Herxheimer reaction alone.

The control of gonorrhea depends upon the treatment of the infected individual and the identification and immediate treatment of all sex contacts. Control of infectiousness is accomplished most promptly by the administration of penicillin in adequate dosage (600,000 units of PAM or benzathine penicillin G) to the contact, immediately, without further proof of infection, but concurrently with taking of blood for a standard serologic test for syphilis. Serologic follow-up once a month for 4 months is advised.

* Available upon request to the Venereal Disease Program, Division of Special Health Services.

It is fairly well established that inadequate treatment for syphilis in its incubation stage will not mask the infection completely, but will prolong the incubation period.

Cases of treatment failure or recurrence of discharge should arouse suspicion of reinfection. Marital and other contacts should be investigated. Wherever possible, contacts should be treated simultaneously to avoid "ping-pong" infections.

## NONSPECIFIC URETHRITIS

An increasing number of cases of what is called nonspecific urethritis, or nongonococcic urethritis, is being reported, especially among members of the Armed Forces. In such cases gonorrhea may or may not have preceded the condition, and certainly the presence of a chronic gonorrheal infection must be ruled out by cultures and other bacteriologic studies. Management of this entity is not standardized, and it requires a combination of good clinical judgment with skill in urologic techniques for a successful therapeutic result. The current literature on the subject should be consulted.

## MANAGEMENT OF SYPHILIS

### Serologic and Other Tests

Syphilis - Diagnosis

Pretreatment laboratory test requirements:
- Primary and secondary syphilis
  - Darkfield examination and serologic tests
- Other stages
  - Serologic tests and spinal fluid examination

In an effort to standardize the technique of the various serologic tests for syphilis, a "Manual of Serologic Tests for Syphilis" was prepared and published. In order that management of syphilis may be adequate, it is suggested that one or more of the techniques described in this Manual be used as standard and that the laboratory procedures be utilized as follows:

For blood specimens. The suggested minimal requirements shall be a single quantitative test on all specimens found positive by the qualitative procedure used.

Darkfield examination. All genital lesions and all extragenital lesions characterized by indolence, induration, and regional lymphadenopathy should be regarded as probable cases of syphilis until all possibility has been excluded by a minimum of 3 darkfield examinations and monthly serologic tests for 4 months.

For spinal fluid specimens. A quantitative procedure from among the spinal fluid techniques given in the Manual is considered a minimal requirement. A cell count should be made immediately after withdrawal of the spinal fluid. Total protein determination can be accomplished advantageously by the trichloracetic acid precipitation method as outlined in the VDRL section of the Manual. The use of colloidal gold or gum mastic tests is optional, although the diagnosis of the type of disease cannot be made from a colloidal test alone.

The darkfield examination is indispensable in the diagnosis of seronegative primary syphilis. In infectious stages of syphilis, darkfield examination is an essential procedure because it enables the physician to arrive at a certain diagnosis within a relatively short time. The demonstration of Treponema pallidum by darkfield examination is conclusive evidence of the presence of syphilis. Treatment should be instituted immediately without waiting for results of a standard serologic test. Practice is required in proper collection of material to be examined as well as in the identification of the organism seen in order to avoid confusion between T. pallidum and the various nonpathogenic organisms, some of which may appear morphologically identical.

Treatment

Syphilis - Treatment

Suggested schedules:

Primary and secondary

PAM - 4,800,000 units (1st injection, 2,400,000; 2nd and 3rd injections, 1,200,000 each; given at 2- to 4-day intervals) or
Benzathine penicillin G - 2,400,000 units in a single injection

Latent, cardiovascular, gummatous, and osseous

PAM - 4,800,000 units (1st injection, 2,400,000; 2nd and 3rd injections, 1,200,000 each; given at 2- to 4-day intervals)

Neurosyphilis

PAM - 10,800,000 units (900,000 every 24 hours for 12 doses)

Early congenital (less than 2 years)

PAM - 1,500,000 units (150,000 every 24 hours for 10 doses)

Late congenital

Same as for comparable manifestations of acquired syphilis

Procaine penicillin G in oil with 2 percent aluminum monostearate (PAM) at the 600,000 units dosage remains at therapeutic level from 72 to 120 hours, while benzathine penicillin G, given in a single injection of 2,400,000 units maintains a therapeutic level for up to 4 weeks.

It is certain that newer preparations having varying absorption properties will be developed. The optimum dosage of each new preparation will have to be determined by treatment evaluation studies similar to those which have resulted in the recommendations given herein.

The administration of penicillin to a person with decompensation due to cardiovascular syphilis is not an emergency, and the demand is to treat the heart first and the syphilis second. The decompensated patient should be given cardiotonic drugs first; then, penicillin may be started in full doses without preliminary heavy metal treatment. If the patient is well compensated, penicillin treatment may be begun immediately since there appears to be no demonstrable risk from penicillin alone in these cases.

Complications such as interstitial keratitis and cardiovascular syphilis in circulatory failure will require specific measures in addition to penicillin. For these, the latest available publications should be consulted. It is recommended that 6,000,000 to 10,000,000 units of PAM be administered so as to maintain an adequate blood level for about 8 days. This should be considered the minimum dose which may be supplemented by additional penicillin or other therapeutic measures as indicated (cortisone in interstitial keratitis, for example). The dosage schedule suggested under neurosyphilis may be utilized.

Under conditions which permit only weekly visits of the patients for treatment or which necessitate discharge of the patient from hospitalization as rapidly as possible, compromises may be necessary in patient management when using PAM. The following schedules (employing procaine penicillin G in oil with 2 percent aluminum monostearate) are considered not ideal but are presented as meeting these exigencies and as having been evaluated to determine their potentialities. They are potentially satisfactory for stages calling for such total dosages.

4,800,000 units - single session (distributed in both deltoid and gluteal regions) or

4,800,000 units - 2,400,000 units at 7-day interval or

9,600,000 units - 2,400,000 units at 7-day intervals or

9,600,000 units - 4,800,000 units at 7-day interval

For treatment of primary and secondary syphilis a single injection of 2,400,000 units of benzathine penicillin G gives results thus far as satisfactory as those obtained with a total dose of 4,800,000 units of procaine penicillin G in oil with 2 percent aluminum monostearate (PAM).

In order to allow more satisfactory contact interviewing and educational opportunities, it is considered advantageous to prolong the contact of patient with clinic beyond the single visit or two required for diagnosis and treatment.

Priorities in Follow-up

Syphilis - Posttreatment Observation *

Primary, secondary, early congenital
- Serologic tests for syphilis (STS) monthly for 6 months; at 9, 12, 18, 24, 36, 48, and 60 months
- Cerebrospinal fluid test (CSF) at 12 and 60 months

Latent, cardiovascular, gummatous, osseous, late congenital
- STS at 6, 12, 24, 36, 48, and 60 months
- CSF at 12 and 60 months

Syphilis in pregnancy
- STS monthly, if possible; essential during last month of pregnancy

Neurosyphilis
- STS at 3, 6, 9, 12, 18, 24, 36, 48, and 60 months
- CSF at 3, 6, 9, 12, 18, 24, 36, 48, and 60 months

* Clinical examination is a necessary accompaniment of laboratory testing at each interval.

If lack of personnel and facilities precludes the follow-up suggested, priorities may be assigned to those requiring the most careful surveillance. Patients originally treated for primary, secondary, congenital, or latent syphilis may be dropped from observation at the 12th month following treatment if they have attained seronegativity (or a fixed low titer in the case of latent or congenital syphilis) and the spinal fluid is negative. There is good indication that seronegativity of blood and spinal fluid at 1 or 2 years after treatment may signify cure of early syphilis. It also has been found that central nervous system involvement after treatment for primary or secondary syphilis is associated with, and usually preceded by, clinical and serologic evidence of reinfection, relapse, or seroresistance.

It must be remembered, though, that the women in the preceding categories who become pregnant need particularly careful observation; that the child with congenital syphilis may develop interstitial keratitis; that we do not yet know about the clinical manifestations of cardiovascular damage which may appear later in life as a result of syphilitic damage to the cardiovascular system prior to bacteriologic cure. Finally, it is well to recall that any patient may become reinfected and that the skin and mucous membrane lesions may then approach, morphologically and histologically, those of late manifestations of syphilis, giving the impression of late relapse rather than reinfection. Reinfection also may manifest itself as development of seropositivity alone without any accompanying lesions.

Latent syphilis showing a slow fall in titer or none at all poses a problem as yet unanswered. However, there is good evidence to indicate that a patient showing no signs of clinical or serologic failure during the first 2 posttreatment years is unlikely to relapse later. These patients may be dropped from observation, if necessary, 2 years after therapy if the spinal fluid tests at the beginning of treatment and at the 12th month following treatment are found to be negative.

It probably is safer to continue the close observation outlined in the first part of the section for patients with late manifestations of syphilis (cardiovascular, central nervous system, etc.) as well as patients slow to revert to negativity following treatment for primary or secondary syphilis.

Re-treatment

Syphilis - Indications for Re-treatment

Primary, secondary, or early congenital
Recurrent lesions; maintenance of STS at or slightly below pretreatment level at 6th month; a fall in titer followed by a rise in titer; positive spinal fluid

Latent or late congenital
In absence of clinical findings, re-treatment is recommended only if sustained rise in serologic titer or spinal fluid positivity is noted

Central nervous system and other late manifestations of syphilis
See detailed discussion in text

Re-treatment schedule:
Double the original dosage is recommended
Repeat spinal fluid examination prior to re-treatment in any stage

In the majority of patients an unsatisfactory course following treatment for primary or secondary syphilis will be obvious.

Certain patients will show persistence of seroreactivity, usually at a low level, i.e., positive or doubtful in dilution of 1:2 or less for long periods. Others will show periods of transient low serologic reactivity, often for no apparent cause, for periods of weeks or months after having been negative. Careful, titered serologic studies are needed to evaluate the status of these patients. Re-treatment on serologic grounds alone, when the patient shows a low titered seroreaction 6 months or longer after treatment should be undertaken only after careful observation by repeated titered STS and clinical evaluation for a period of several months. However, if close observation is impossible, patients with a serologic titer of 8 or more Kahn units or equivalent 12 months after treatment for primary or secondary syphilis should be re-treated.

In latent and late syphilis, maintenance of the serologic titer at or the slow fall below the pretreatment titer is not considered an indication for re-treatment. However, a sustained rise in serologic titer of 2 tubes or more may indicate need for re-treatment. In neurosyphilis, if an "active" spinal fluid formula does not revert to negativity or inactivity (normal cells and protein), if an inactive spinal fluid shows reversion to activity (increased cell count, protein, rise in titer), or if there is clinical evidence of failure or relapse, re-treatment is indicated.

Cases With Doubtful Diagnoses

It is anticipated that there will be seen an increasingly large number of patients who have a positive or doubtful STS as the sole referring complaint. In this group, a Treponema pallidum immobilization (TPI) test may be found helpful when considered in the light of a complete study of the patient.

Such a patient with no history of syphilis requires a complete examination, including spinal fluid examination, to determine the significance of the serologic findings and may require prolonged observation including repeated serologic testing before a definite diagnosis can be given. A woman late in pregnancy, under these conditions, should be treated as a precaution; others should be studied thoroughly over a period of time.

The patient referred for possible re-treatment with a positive STS and who gives a history of an apparently adequate course of therapy with either penicillin or arsenic and bismuth requires careful evaluation of his physical and serologic status before administration of further therapy in order to obviate needless re-treatment. The possibility of seroresistance always must be considered.

Marriage

Permission to marry following treatment must be based upon an understanding of the infectiousness of the patient, not merely upon presence or absence of a positive STS.

In primary and secondary syphilis permission may be given upon attainment and maintenance of seronegativity for at least a month. If the individual shows an unusually slow rate of reversal, permission safely may be granted upon achievement and maintenance of a low serologic titer, 6 or more months after treatment.

The adequacy of treatment must be considered in the final decision.

In latency or late symptomatic syphilis, permission must be based upon evaluation of adequacy of treatment and consideration of the patient's status, for seroreversal usually cannot be expected.

The diagnosis should be made known to both applicants when one of them has late syphilis; this is especially important in central nervous system syphilis.

Reporting

All cases of syphilis should be reported to the State health department. Morbidity reporting enables State and local health departments to estimate the extent of the local venereal disease problem. Reporting of cases to local health officers allows them to provide the reporting physician with any available services necessary to assure maximum protection of public health and to assist in management of the case. Morbidity reporting also provides a basic index for measuring the success or failure of venereal disease control programs.

## MANAGEMENT OF SAPROPHYTIC SPIROCHETAL BALANITIS

Saprophytic spirochetal balanitis is suggested when the darkfield examination of superficial and dirty penile erosions reveals large numbers of saprophytic spirochetes. Even though a few organisms morphologically similar to T. pallidum are present, the diagnosis of syphilis should not be made so long as they are found associated with the obviously nonpathogenic spirochetes. If the STS is negative, a local application of 2 cc. of aqueous penicillin solution of 20,000 units per cubic centimeter should be made for 10 to 15 minutes on two successive days. If the lesion is nonsyphilitic, healing takes place within several days.

If syphilitic, the saprophytic organisms will be eliminated so that within several days after the application T. pallidum will be present again and can be identified unequivocally.

The patient should return for a monthly STS for 4 months following treatment. He should be warned to report promptly if lesions develop. The need for cleanliness should be stressed.

## MANAGEMENT OF CHANCROID

Chancroid

Diagnostic aids:
- Ducrey vaccine skin test
- Darkfield and STS (sufficient series to rule out syphilis)

Treatment:
- Sulfadiazine is the drug of choice - 1.0 gm. 4 times a day for 7 days
- Certain of the antibiotics have been found effective in dosages as follows
  - Streptomycin or dihydrostreptomycin - 0.5 to 1.0 gm. intramuscularly 4 times per day for 5 to 7 days or
  - Aureomycin - 0.5 gm. orally 4 times per day for 7 to 14 days or
  - Chloramphenicol - 0.5 gm. 4 times per day intramuscularly for 13 days

Follow-up:
- If lesion does not heal, the diagnosis of syphilis, granuloma inguinale, or malignancy should be reconsidered and investigated carefully. In some cases, a longer course of the drug or a change of drug may prove necessary

Serologic test for syphilis monthly for 4 months

All patients with genital lesions should have a series of STS and Darkfield examinations adequate to rule out or confirm the diagnosis of syphilis. Mixed infections with more than one venereal disease may appear in one patient simultaneously, even in the same lesion.

A positive skin reaction to the Ducrey vaccine is present in most patients with chancroid of 8 or more days' duration, and indicates a past

or present infection. This test should be given and the reaction interpreted according to instructions received with the antigen used. Since the skin test frequently is negative early in the disease, the differentiation of chancroid from syphilis largely is through exclusion of syphilis (by darkfield and STS) and other diseases causing similar lesions.

Culture and smear are of limited value and are not recommended routinely.

Local treatment should consist of cleanliness. Inguinal buboes should not be incised but may be aspirated through normal skin with a #15 or #16 needle if fluctuant.

## MANAGEMENT OF GRANULOMA INGUINALE

Granuloma Inguinale

Diagnosis:
Finding the Donovan body in scrapings or biopsy material
Darkfield and STS (sufficient series to rule out syphilis)

Treatment:
Streptomycin or dihydrostreptomycin - 1.0 gm. intramuscularly 3 times a day for 7 to 10 days or
Aureomycin, terramycin, or chloramphenicol, orally - 500 mg. 4 times a day for 12 1/2 days or
Chloramphenicol - 4 gm. intramuscularly every 3 to 7 days for 3 doses

Treatment resistance or relapse:
Requires prolongation of therapy or change of antibiotic agent

Follow-up:
If lesion fails to heal or relapse occurs, a larger and longer course of therapy or change of antibiotic may be required. Malignant change must then be ruled out

Serologic test for syphilis monthly for 4 months

Granuloma inguinale should be suspected in patients with granulomatous lesions in the genital area. Any lesions on the genitalia or perineum, especially on swollen vulvae, are suspect if found darkfield negative and seronegative, and a search for Donovan bodies should be instituted.

Care should be taken to go deep for a biopsy specimen or to assure that the surface has been cleared of secondary invaders by appropriate nonspecific local medication prior to taking specimens for study. Tissue, not exudate, should be examined for demonstration of Donovan bodies.

Local therapy may be found to hasten healing of certain ulcers. In some chronic cases especially in the female with scarring, swelling, and deformity, surgery may be indicated in addition to specific antibiotic therapy.

## MANAGEMENT OF LYMPHOGRANULOMA VENEREUM (LGV)

Lymphogranuloma Venereum (LGV)

Diagnosis:
Frei test (suggestive but not conclusive)

Treatment:
Sulfadiazine is the drug of choice - 1.0 gm. 4 times a day for 12 to 15 days
Satisfactory results have been reported with antibiotics in these dosages:
Aureomycin, terramycin, or chloramphenicol, orally - 500 mg. 4 times a day for 5 to 10 days or longer as indicated by clinical response
Chloramphenicol - 2 gm. intramuscularly daily for 6 days

Follow-up:
If lesion does not heal, the possibility of coexistence of another disease or of erroneous diagnosis must be investigated. Prolongation of therapy or change of drug may prove necessary in some cases

Serologic test for syphilis monthly for 4 months

Acute or indolent inguinal adenitis with or without the finding of inconspicuous vesicular genital lesions should suggest the diagnosis of LGV. The finding of a positive Frei test is suggestive but not conclusive evidence of the diagnosis because it may be from a previous infection. Routine performance of complement-fixation test for LGV is not recommended. The clinical finding of acute inguinal adenitis, unaccompanied by genital lesions, usually is highly suggestive and is sufficient to permit administration of sulfonamide therapy. However, a differential diagnosis must be considered and investigated if there is not a rapid response to specific therapy. The chronic manifestations of LGV frequently enter into the differential diagnosis of other venereal diseases, as well as certain gynecologic, genitourinary, and proctologic conditions. For these, one should refer to standard texts.

Fluctuant buboes should be aspirated through normal skin with a #15 or #16 needle but they never should be incised because of the slow healing which follows incision. Local treatment should consist of cleanliness, and the lesion should be left dry. The chronic manifestations such as esthiomene or rectal stricture call for appropriate medical and surgical management.

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